UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM November 23, 1999

SUBJECT: REVISED Propargite Quantitative Risk Assessment (Q_1^*) Based On Sprague-Dawley Rat Dietary Study Using mg/kg b.w.^$^3/_4$'s/day Cross Species Scaling Factor

P.C. Code 097601

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The revised upper bound estimate of unit risk, Q_1^*(mg/kg/day)$^{-1}$, of Propargite based upon male rat fatal jejunum sarcoma tumor rates is 2.01 x 10^{-1} in human equivalents. The dose levels used from the 105-week dietary study were 0, 50, 80, 400, and 800 ppm of Propargite. The corresponding tumor rates were 0/42, 0/46, 0/44, 11/44, and 24/45, respectively.

Background

On February 12, 1992, the Cancer Peer Review Committee classified Propargite as a Group B2 - probable human carcinogen, and recommended that, for the purpose of risk characterization, a low dose extrapolation model be applied to the experimental animal tumor data for quantification of human risk (Q_1^*). A Q_1* was generated using mg/kg b.w.^$^3/_4$'s/day cross species scaling factor (Propargite (Omite) - Revised Q_1^*, ($^3/_4$'s Interspecies Scaling Factor), Sprague-Dawley Rat Dietary Study, B. Fisher and H. Pettigrew, 2/16/95). However, the tumor ratios in this memo do not agree with the tumor counts provided in the qualitative memo (Propargite (Omite), Qualitative Risk Assessment - Sprague-Dawley Rat Dietary Study, B. Fisher, 1/15/92), and no explanation is provided to account for the discrepancies. This revised memo has been generated to reflect the original tumor counts using the

$^{3}/_{4}$'s scaling factor, as changed from the $^{2}/_{3}$'s by Agency policy in 1994[1].

All unit risks have been converted from animals to humans by use of the $^{3}/_{4}$'s scaling factor (Tox_Risk program, Version 3.5, K. Crump, 1994)[1]. For the conversion to human equivalents, weights of 0.35 kg for the rat and 70 kg for humans were used.

It is to be noted that the Q_1^* $(mg/kg/day)^{-1}$ is an estimate of the upper bound on risk and that, as stated in the EPA Risk Assessment Guidelines, "the true value of the risk is unknown, and may be as low as zero."

Dose-Response Analysis

On September 7, 1999, Uniroyal Chemical Company submitted Comments on HIARC Determinations On Propargite Toxicity. On page 6, this document questions the Agency's exclusion of animals that died before week 65 from the analysis. It is the Agency's policy to exclude animals that die before observation of the first tumor, week 65 in the case of the male rat jejunum sarcoma tumors, from any analyses where there are significant survival disparities among the dose groups. Since the statistical evaluation of mortality (Propargite (Omite), Qualitative Risk Assessment - Sprague-Dawley Rat Dietary Study, B. Fisher, 1/15/92), indicated a significant increasing trend with increasing doses of Propargite in male rats, the Peto prevalence test was used to analyze the male rat tumors. The unit risk, Q_1^*, was obtained by the application of the time-to-tumor Weibull model (Tox_Risk program, Version 3.5, K. Crump, 1994).

Male rats had a significant increasing trend, and significant differences in the pair-wise comparisons of the 400 and 800 ppm dose groups with the controls, for fatal jejunum sarcoma tumors, all at $p < 0.01$.

[1]See memo - Deriving Q_1^*s Using the Unified Interspecies Scaling Factor, P.A. Fenner-Crisp, Director, HED, 7/1/94.